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Discussion

Dr Frank L. Hanley *(Stanford, Calif).* Congratulations, Dr Carotti, for a very nice presentation and congratulations to you and your colleagues for an outstanding series.

Consensus regarding the management and outcomes of patients with pulmonary atresia and collaterals has been hard to come by. This study from Bambino Gesú Children's Hospital adds to a growing international experience that is allowing some consensus to finally emerge. This study, along with other notable large series with careful midterm follow-up, such as the 500-or-so plus cases from the Stanford group and the roughly 300-or-so from the Birmingham, England, group, to name just a few, now provide an international multiple center experience that is approaching 1000 cases or more and provide a fairly clear picture regarding some very important points with respect to this lesion.

The 3 major conclusions that I think we now pretty much have a consensus on are the following:

First, when unifocalization is performed aggressively and relatively early in life according to strict protocols coupled with intracardiac repair, midterm outcomes can be achieved that improve quite dramatically on the natural history of the disease.

Now, that might not sound like much of a comment. However, it is notable that as recently as 5 to 10 years ago, and even up to this present day, the question of whether surgery improves on the natural outcome has been seriously debated. Now, there is absolutely no question that surgery improves the outcome.

I would go one step further and say that protocols such as yours, which is very close to our protocol and quite close to, I think, Dr Brawn's protocol, also provide probably the best outcomes relative to other alternative, competing surgical procedures.

The second point that I think we have a consensus on is that collateral arteries when unifocalized correctly contribute importantly, even critically, to a durable, growing, healthy pulmonary vascular bed. Your excellent outcomes in this series with patients with completely absent native pulmonary arteries, that is, those patients whose pulmonary vascular bed was reconstructed solely from the collateral arteries, reflects our own program's experience pretty much exactly and underscores this point, that collaterals clearly are very important.

The third major point is the following: ''Tending the garden,'' if you will, that is, frequent assessment of, and surgery and catheter-based management of, the reconstructed pulmonary vascular bed are all extremely necessary parts of the long-term treatment of these patients. Again, I think there is a growing consensus about that.

These points of consensus notwithstanding, many differences remain in individual institutions with respect to the specifics of the management protocols and the identification of the various risk factors. Also, clearly, we cannot go into all of those nuances and variations in this short period. I do want to focus on one area.

Your outcomes are outstanding. If you eliminated the one subgroup, the mortality in the one subgroup (i.e., those who had undergone complete unifocalization and failed the flow study and did not have VSD closure), if you eliminated the mortality, or equaled the mortality, in that subgroup as in all your other subgroups, your outcomes would be phenomenal. So that is where I want to focus.

I notice that you identified VSD closure as a risk factor for mortality. In the 25 patients in that subgroup, complete unifocalization without VSD closure, 6 patients died. I was wondering whether you could say a few things about your insights into that subgroup and specifically address the following questions:

When you do the flow study, what criteria for the flow study do you use specifically to make that decision? Because that might affect on why some of them were not doing well.

Second, and, perhaps, even more importantly, in this answer to this question, how do you provide the pulmonary blood flow, because you were not closing the VSD? Do you use a shunt? Do you use some form of right ventricle-pulmonary artery (RV-PA) connection? Do you put a VSD patch on and then fenestrate it? What are your thoughts on that?

Dr Carotti. Thank you very much for your comment and for your questions.

Regarding the pulmonary flow study, we perform it exactly as we learned from you in 1996 when we visited your center. We use a derivation from the arterial port of the oxygenator to perfuse the pulmonary vascular tree with oxygenated blood. We cool down the patient to a nasopharyngeal temperature of 25°C. We keep the hematocrit at 25%. Then, with the heart beating, we perfuse the pulmonary arterial tree by incremental steps up to 100% of the cardiac index and record simultaneously the mean pulmonary arterial pressure changes. We rely on a cutoff value of 30 mm Hg and decide to close the VSD as long as the mean pulmonary arterial pressure remains within such a value. For any pressure value exceeding 30 mm Hg, we leave the VSD untouched and provide pulmonary blood flow using a RV-PA conduit with the VSD left open. In a couple of patients with the VSD left open, we banded the conduit because of a progressive increase in the arterial oxygen saturation, to avoid overperfusion of the pulmonary arterial bed.

We never perform primary closure of the VSD using a fenestrated patch. However, in our early experience, we had 2 patients who developed hypersystemic right ventricular pressure after VSD closure despite falsely reassuring pulmonary flow study findings. In both cases, we decided to fenestrate the patch, and those were the only patients who ended up with a fenestrated VSD patch closure.

Regarding the use of a systemic pulmonary shunt, we did it once in our very early experience by replacing the conduit originally implanted. However, that patient died. At the postmortem, she had diffuse pulmonary vascular disease. She was a 12-year-old child. After this unsuccessful experience, we have always preferred to perform right ventricular outflow tract reconstruction to provide blood flow to the lungs.

Dr Hanley. So I think I would summarize what I am getting from your answer, that you do pretty much a standard flow study with well-recognized parameters for deciding when to close a VSD.

Just for the sake of argument, we, in our program, we never open the right ventricle unless we are going to close the VSD. Thus, everybody who fails a flow study receives a well-controlled shunt, in an attempt to achieve a mean pressure of 25 mm Hg in the pulmonary arteries.

Now, I do not know whether that enters into why you had a 6 of 25 patient mortality. Not that that is terrible. I mean your results overall are outstanding. But this is a sort of the hot spot where you had a few little problems. We originally used RV-PA conduits early in the game. By 2000, we had switched completely to shunts when the flow study failed because we were having complications with the systemic level RV-PA conduits and the ability to really control the blood flow in the lungs really well.

Again, when creating a ventriculotomy, pulmonary insufficiency is going to be present chronically and also pseudoaneurysms, et cetera. All those things we found to be concerns. I do not know whether the shunt makes the difference. It is a relatively small number and it might not, but I am just pointing out some differences.

Dr Carotti. To corroborate what you say, in our experience, a few patients with the VSD left open died because of massive pulmonary hemorrhage, likely secondary to uncontrolled pulmonary blood flow. In our mind, the most appealing reason to have an RV-PA conduit providing forward flow is the optimal access for percutaneous interventions, which might enhance the perspectives of subsequent VSD closure. Actually, most of our patients who experienced massive pulmonary hemorrhage had chromosome 22q11 deletion, which remains an important risk factor for death in our analysis, and we were more keen to correlate the airway bleeding to the syndrome itself than to the uncontrolled pulmonary blood flow. Anyway, I take your suggestion.

Dr Hanley. Then, a second very brief question. I noticed in your manuscript, and I think in the presentation as well, the mean age at which you performed unifocalization was 15 months. Now, I know very well, as you do, when you are getting referrals, you cannot control the patient's age all the time. I also wonder whether that slightly older age might have had something to do with some of those patients who had variable pulmonary blood flow with perhaps slightly sick pulmonary microvascular systems because of the long-term flow, up to 15 months. Again, the analogy I usually make is you would never let a truncus go 15 months before you would repair it. You know the patients are going to have pulmonary vascular problems. I know you cannot control the age. Left in the ideal situation, if you were referred a newborn, when would you perform the unifocalization?

Dr Carotti. When the body weight is 5 kg.

Dr Sabine Daebritz *(Duisburg, Germany).* Thank you for this very interesting talk.

Can you briefly comment on the criteria you used to decide when to close the VSD once you had left it open.

Dr Carotti. Yes. Thank you first for your question.

We do rely only on the intraoperative pulmonary flow study and on a mean pulmonary arterial pressure cutoff value of 30 mm Hg. If we reach up to 30 mmHg for the mean pulmonary arterial blood pressure during flow study, we go ahead and close the VSD. Otherwise we leave the VSD open.

Dr Tweddell. I think she is asking, in those patients, when you leave it open, when do you subsequently go back and close it?

Dr Carotti. I am sorry, I did not understand.

Usually, we restudy those patients about 12 months after the operation and see what the pulmonary blood flow/systemic blood flow (Qp/Qs) ratio is. In the absence of significant stenosis at the distal anastomosis of the conduit, or at the unifocalization site, we accept a Qp/Qs ratio greater than 1.5:1 to proceed with VSD closure. Otherwise, we could accept an even lower Qp/Qs ratio in the presence of significant stenoses, which would be treated at operation.

What we learned from our most recent experience is that those patients react during catheterization also to hyperoxia and nitrous oxide administration. In the last couple of patients with a basic Qp/Qs ratio of 1:1, hyperoxia increased the Qp/Qs ratio to 2:1 and nitrous oxide to 2.5:1. So we are also doing vasoreactivity functional tests when we restudy such patients.

Dr Tweddell. When you do the flow study, what index do you target?

Dr Carotti. 2.5 L/min/m^2.

Dr Tweddell. Thank you very much.